**AS Unit 1: Basic Biochemistry and Cell Organisation**

| Name: | Date: |
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## Topic 1.2 Cell Structure and Organisation – Page 6

### I. Viruses

| | | Completed |
|---|---|---|
| 1. | Read about the structure of viruses as seen under the electron microscope.<br>• Rowlands p32<br>• Toole p<br>• **Handout 1.2M Bio Factsheet Viruses Made Simple** | |
| 2. | Complete the questions at the end of **1.2M** | |
| 3. | Find out about the Ebola virus.<br>• What type of virus is it?<br>• How is it spread?<br>• What is being done to contain its spread?<br>• What treatments are available? | |

Bio Factsheet

September 1998 Number 32

# Viruses made simple

**Viruses lack the mitochondria necessary to derive energy and they cannot reproduce on their own. They are dependent on their host cells and are only classed as living organisms when they infect host cells. After reproducing, viruses inevitably cause their host's destruction. It is because of these characteristics that viruses are described as obligate intracellular parasites. This Factsheet will describe the structure of different types of viruses, their life cycles and their pathogenic (disease causing) properties.**

## Classification of viruses.

Viruses can be classified according to characteristics such as:

(a) The disease they cause e.g. influenza
(b) Their tissue target e.g. neuronal
(c) The vector by which they are transmitted

However, the most widespread classification schemes are based on viral structure, for example:

(a) Their nucleic acid (DNA or RNA)
(b) Their size
(c) Their **morphology** (shape and structure)

**Common exam questions**

1. Why can viruses be classified as living and non living?
2. Explain why all viruses are considered to be parasites.

## Size of viruses

Viruses range in size from the smallest picornaviruses (20 nanometres) to the largest poxviruses (350 nanometres). Note, however that they are much smaller than bacteria.

## Virus morphology

The virus core consists of nucleic acid, which may be associated with accessory proteins such as enzymes. Surrounding the nucleic acid is a protein coat called a **capsid**. Before assembly with the nucleic acid and accessory proteins, the empty protein shell is called a **procapsid.** After the components have assembled, the structure is called a **mature capsid.** Viruses with no other features are referred to as **naked capsid viruses**. Alternatively the capsid may be surrounded by a membrane composed of lipid, proteins and glycoproteins, in which case the particle is described as an **enveloped virus.**

The morphology of the capsid can be described as follows:

(a) **Helical**
(b) **Icosahedral** (a icosahedron is a 20 faced solid)
(c) **Composite** (having helical and polyhedral components)

Examples of such structures are shown in Fig 1.

## Replication of viruses in general

Viruses identify the cells which they attack by recognising specific cell surface receptors. For this reason viruses will usually only infect one species. In simple terms, when a virus infects a cell it injects its own genetic material (**either** DNA or RNA) into the cell. The genetic material of the virus then replicates and many new virus particles are assembled. The replicating virus uses the host cell's nutrients and energy sources, preventing the cell carrying out normal metabolism. Finally, the cell is destroyed and the virus particles are released and are able to infect new cells. Viruses which infect bacterial cells are called **bacteriophages**, those that infect animals and plants are called animal and plant viruses respectively.

## Replication of bacteriophages

Bacteriophages, or phages as they are commonly called, undergo two types of replication: **lytic and lysogenic**. Fig 1(c) shows the T4 phage, an example of a lytic bacteriophage.

### (a) Lytic replication e.g. T4 phage

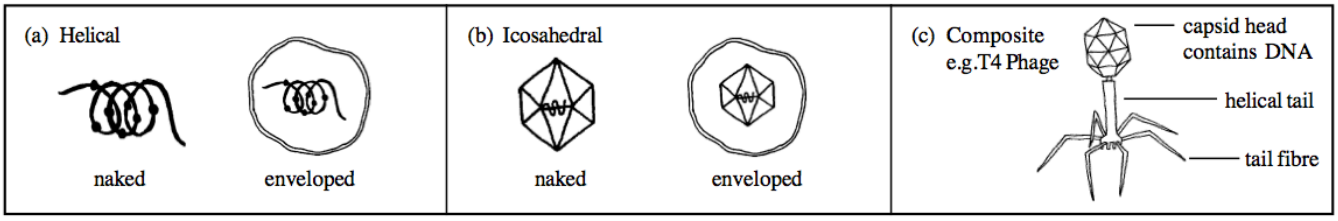
The first stage of lytic replication is the **adsorption** (attachment) of the phage to the bacterial cell. Following adsorption, the tip of the phage tail becomes attached to a specific cell surface receptor. The sheath of the tail then contracts, puncturing the bacterial cell wall and membrane, thus enabling the phage genome (DNA) to be injected into the bacterium.

Following penetration, the DNA of the phage is transcibed (i.e. used as a template for mRNA synthesis) and the bacterial DNA is degraded. The mRNA is translated by the bacterial cell (i.e. proteins are synthesised according to the instructions given by the mRNA template).

Once the structural proteins and nucleic acid have been synthesised, the phage components are assembled into mature capsids. After approximately 25 minutes some 200 phages are assembled, leading to **lysis** (disintegration) of the bacterial host and the release of new viruses, which in turn infect other bacteria. The cycle then repeats.

***Exam Hint*** *- Some Examination Boards require you to know the difference between the lytic and lysogenic cycles. It is easy to confuse the names but they are two very different processes.*

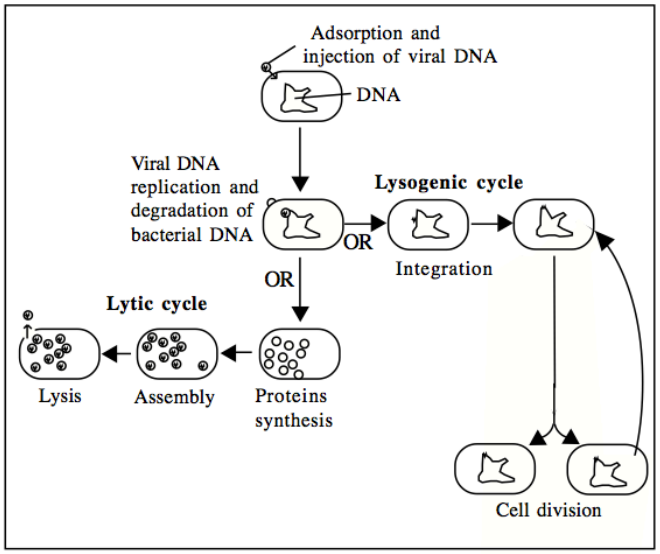
**Fig 1. Examples of capsid structures**



(b) **Lysogenic replication e.g. Lambda (λ) phages**

In addition to lysis, some types of viruses can replicate by incorporating their DNA into the host DNA. This type of replication is called lysogeny. A lambda phage is an example of a virus which replicates by lysis and lysogeny. In its incorporated form, the lambda phage genome is called a prophage. Subsequently, the phage DNA is transmitted to each bacterial daughter cell as the cells reproduce. During lysogeny the phage also produces a protein which inhibits the lytic cycle but ensures the integration of the phage DNA into the bacterial DNA. Under certain conditions - such as exposure to UV light - the lytic cycle of the lambda phage is initiated. UV light stimulates the production of a bacterial cell protein which cleaves the repressor protein produced by the phage. Since the lytic cycle is no longer inhibited, the viral particles are assembled and the bacterial cell lyses. Fig 2 shows a flow diagram to represent both the lytic and lysogenic cycles.

**Fig 2. The lytic and lysogenic cycles**



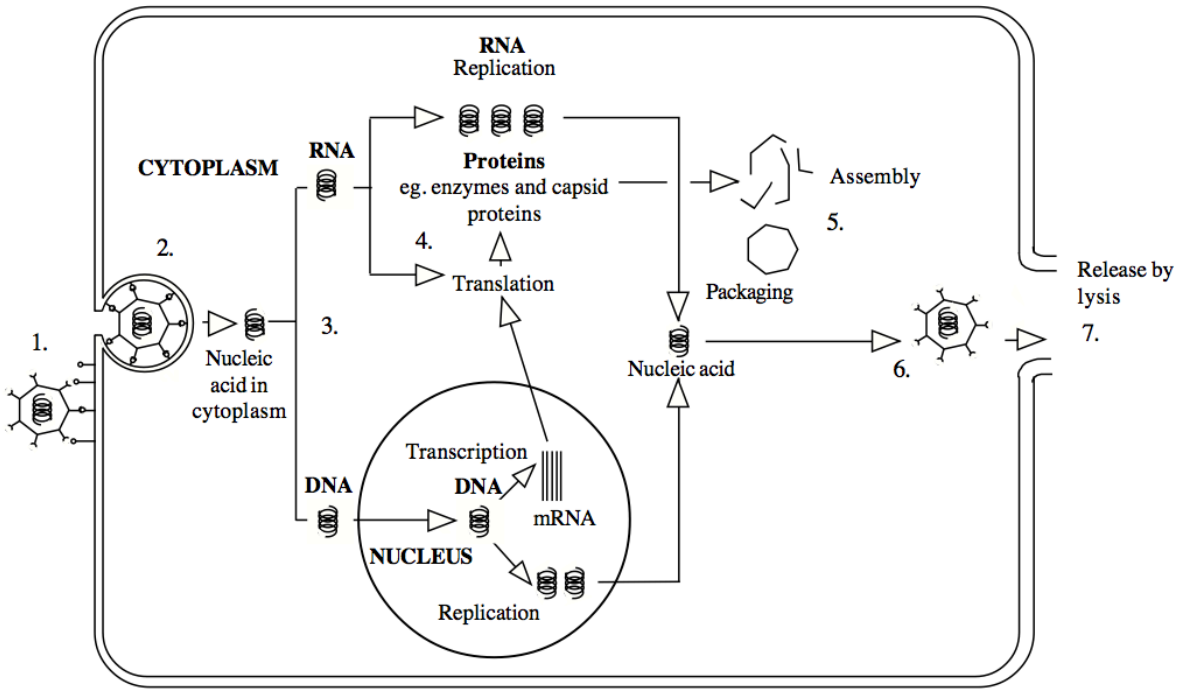

**Replication of animal viruses**

Infection of the host with an animal virus leads to a variety of effects, including lysis of the host cell, **latency** (where the virus exists in cells but is not replicating) and **host cell transformation** (a change in the structure or properties of the host cell), which together with genetic and environmental factors, leads to the formation of a tumor. The general life cycle of an animal virus is shown in Fig 3. The virus shown is a naked capsid virus.

1. Recognition and attachment (receptors on the surface of the virus recognise and attach to receptors on the surface of the host cell).
2. Penetration of the host by endocytosis.
3. Uncoating of the viral genome (DNA genomes are usually transported to the nucleus and RNA genomes usually remain in the cytoplasm).
4. Synthesis of nucleic acid and proteins (using the host cell's endoplasmic reticulum).
5. Viral assembly.
6. Viral packaging.
7. Release of new viral particles by lysis (naked capsid viruses).

***Exam Hint*** *- Remember that DNA is replicated in the nucleus and RNA is usually replicated in the cytoplasm.*

**Fig 3. The general life cycle of an animal virus (DNA or RNA).**



### Replication of plant viruses

All plant viruses are RNA viruses. Plant viruses enter their hosts through damaged regions of the plant or by insect bites which transport the viruses into the host cells. Once the virus has infected the host cell, replication is the same as an animal RNA virus. Firstly, the capsid is removed and then the RNA is transcribed and replicated to make mRNA and new RNA genomes. The viral proteins are then translated from the mRNA.

Once the RNA genome and proteins have been synthesised, the protein coat surrounds the newly formed nucleic acid in a self-assembly process. Tobacco Mosaic Virus (TMV) is an example of a plant virus. Within the plant, the TMV particles form crystalline structures and infected regions become yellow (**chlorotic**) due to the loss of chlorophyll. The leaves of such infected plants develop characteristic mosaic patterns of chlorosis. Ultimately, the completely assembled virus particles and any unpacked viral nucleic acid molecules are released as the plant dies.

Plant viruses commonly cause symptoms such as leaf mosaic (yellow mottling of leaves), crinkled leaves and stunted growth. The subsequent reduction in yield is of great economic importance. Some significant examples are outlined below (Table 1).

**Table 1. Example of plant viruses.**

| Disease | Symptoms | Virus | Transmission |
|---|---|---|---|
| **Tobacco Mosaic Disease** | Yellow-brown mottled leaves | Tobacco Mosaic Virus, Elongated | Fungus, Grafting, Mechanical damage |
| **Tobacco Rattle Disease** | Dry, brown, papery leaves | Tobacco Rattle virus, Elongated | Nematode worms |
| **Tomato Spotted Wilt** | Wilting, spots of discolouration | Tomato Spotted Wilt Virus, Spherical and enveloped | Thrips |
| **Turnip Yellow Mosaic Disease** | Yellow mottled leaves | Turnip Yellow Mosaic virus, Spherical | Beetle |

### Viruses as pathogenic agents

Many viruses act as pathogenic (disease causing organisms) in humans (Table 2).

**Table 2. Examples of animal viruses & their symptoms**

| Disease | Symptoms | Virus | Transmission |
|---|---|---|---|
| **AIDS** | Weight loss, Diarrhoea, Dementia, Kaposi's sarcoma | Human Immunodeficiency Virus (HIV), RNA containing retrovirus, Spherical and enveloped | Sexual intercourse, Blood transfusion, Sharing needles, Transplacental |
| **Common Cold** | Runny nose, Sneezing, Coughing | RNA containing rhinovirus (of which there are many strains), Icosahedral and enveloped | Droplet infection |
| **Genital Herpes** | Genital ulcers, Fever, Swollen glands | Herpes Simplex type 2, DNA containing, Icosahedral and enveloped | Across urogenital tract via sexual contact |
| **German Measles (Rubella)** | Rash, Malaise, Foetal abnormalities | Rubella Virus, RNA containing, Icosahedral and enveloped | Droplet infection |

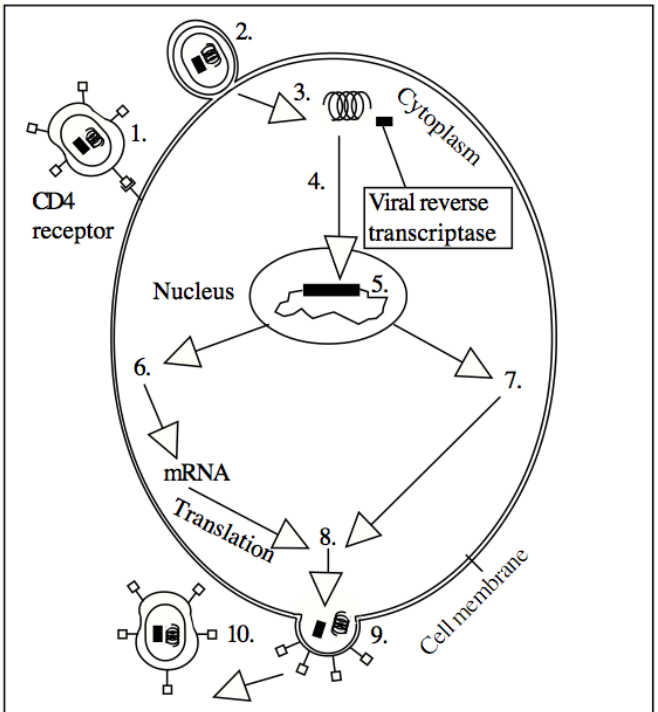
### Retroviruses

Retroviruses contain RNA and an enzyme called **reverse transcriptase** which catalyses the production of single stranded DNA, called **copy DNA** (cDNA) from the RNA template. The cDNA then acts as a template for a second strand, thereby forming double stranded DNA which is integrated into the host cell chromosomes. This is referred to as **proviral DNA.** When the host cell divides the proviral DNA is transmitted to the daughter cells.

HIV (Human Immunodeficiency Virus), the virus responsible for the disease AIDS (Aquired Immune Deficiency Syndrome) is a retrovirus which infects T-lymphocytes of the immune system (Fig 4). The virus can remain latent for many years before it is activated to start replicating and destroy its host cell. By reducing the number of T-lymphocytes, HIV weakens the body's ability to fight infection. Eventually, individuals who are carrying HIV succumb to a range of **opportunistic infections** - so called because they usually only affect people whose immune system is weakened. AIDS (acquired immune deficiency syndrome) is the name given to this collection of unusual, opportunistic diseases.

Thus, AIDS is not a single disease, but a descriptive term for the opportunistic infections. People who develop AIDS often die from Karposi's sarcoma, a rare cancer itself caused by a virus.

**Fig 4. The replication process of the HIV virus.**




1. Attachment of retrovirus to CD4 receptor.
2. Fusion of viral membrane with host cell.
3. Viral RNA.
4. Action of reverse transcriptase leads to formation of single strand DNA and subsequently double stranded DNA.
5. DNA intergrated into host cell chromosone. Now called proviral DNA.
6. Transcription of viral DNA to form mRNA.
7. Synthesis of viral genome using mRNA.
8. Proteins are processed and together with genomic RNA. New viral progeny are as sembled.
9. Budding of virus.
10. Mature viral particle

### Treatment of viral infections

Treatment of viral infections is difficult because the infections take place inside cells where it is difficult to reach. It is also difficult to find a drug which specifically targets the virus and not the host cells, since the virus uses the host cell's nutrients and energy to replicate. Unfortunately, treatment which successfully inhibits the replication of the virus often inhibits and damages the infected cells.

However, in recent years many drugs have been developed which are selectively activated in infected cells because the viral particles convert the drug from an inactive form to an active form. Different viruses possess different enzymes which can activate drugs. **Aciclivor** - the active ingredient in Zovirax, the cold sore cream - is a good example. The general principle is that different viruses possess different enzymes which can activate drugs. Thus, selectivity towards different viruses is also possible.

### Vaccines

The **antigenic components** of viruses (those recognised as foreign by host cells), such as their cell surface receptors, can provide **protective immunity** for the host. The host's immune system produces antibodies which recognise the viral antigens, thus enabling the host to selectively destroy any similar particles. This is the basis of **vaccines**, which usually consist of **attenuated** (weakened) antigens, which are injected or ingested into the host. The host's immune system produces antibodies against this antigen and the host is immunised, usually without suffering any symptoms.

However, vaccinations impose a selective pressure on viral antigens. This leads to changes in their structure and inevitably, the formation of new viral strains. New strains are also formed by **mutation** (a change in the structure of the genome). Viruses such as HIV mutate and change structure very quickly and cannot therefore be treated by vaccines.

### Using viruses in the laboratory

The two most common reasons for producing a virus in large numbers are to investigate its pathogenic (disease causing) properties or to study its structure closely. Most viruses are pathogenic and therefore special conditions are needed for their use in the laboratory. Viral work is performed in purpose built cabinets, similar to fume cupboards, and protective clothing such as safety gloves and lab coats are worn. Viral culture is usually carried out by inoculating (infecting) cells kept alive in a nutrient rich solution,usually fertile eggs or embryos. After inoculation, the infected cells or tissues are incubated, whilst the virus reproduces.

Equipment can be disinfected by using liquids e.g.

(i) Alcohols
(ii) Phenolic compounds

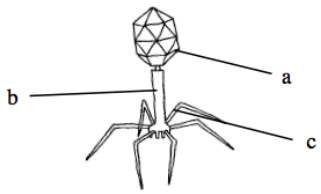
Equipment can be decontaminated by sterilisation using:

(i) Heat e.g. autoclaving in steam under pressure at 121°C
(ii) Liquids e.g. hydrogen peroxide or formaldehyde

Viruses are stored at temperatures between -20°C to -70°C.

### Practice Questions

1. Fig 1. shows a diagram of a bacteriophage




Label structures a, b and c. (3 marks)

2. Name two features which are characteristic of all viruses. (2 marks)

3. Animal viruses can be grown by inoculating them into cells of mature animals. Name two other methods for growing animal viruses. (2 marks)

4. Tobacco rattle virus is a pathogen affecting tomato plants and is transmitted by nematode worms.

   (a) Suggest why the tobacco rattle virus cannot penetrate leaf cells without the aid of nematode worms. (1 mark)

   (b) Suggest why the virus does not replicate in the nematode worm. (1 mark)

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*This Factsheet was researched and written by Nirinder Hunjan*
***Curriculum Press, Unit 305B, The Big Peg,***
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